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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/746,921	12/22/2000	Kevin J. Thorne	2265-15	2764
45488	7590	07/27/2005	EXAMINER	
WILLIAMS, MORGAN & AMERSON, P.C./ZIMMER 10333 RICHMOND, SUITE 1100 HOUSTON, TX 77042			LEITH, PATRICIA A	
			ART UNIT	PAPER NUMBER
			1655	

DATE MAILED: 07/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/746,921

Applicant(s)

THORNE ET AL.

Examiner

Patricia Leith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 June 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 24-29 and 32-48 is/are pending in the application.
4a) Of the above claim(s) 9 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-8, 10, 24-29 and 32-48 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/11/05 has been entered.

Claims 1-10, 24-29 and 32-48 are pending in the application.

Claim 9 was withdrawn from examination on the merits as it is directed toward a non-elected invention.

Claims 1-8, 10, 24-29 and 32-48 were examined on their merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office Action.

Claim Rejections - 35 USC § 103

Claims 1, 3-5, 8, 10, 24-27, 32-48 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ohura et al (1999) in view of Chen et al. (US 5,707,962).

Applicant's arguments were fully considered, but not found persuasive.

Applicant argues that "Neither Ohura nor Chen teaches or suggests acidic pHs that are capable of enhancing bone growth protein induced bone formation" (p. 8, Arguments). However, it is clear on the record that Ohura et al. taught MCMP, an acidic monophosphate. Because MCMP is acidic, it is deemed that MCMP makes obvious this embodiment of the claimed invention. One of ordinary skill in the art would have been motivated to incorporate MCMP into a bone growth formulation comprising a substrate and a bone growth protein, because all of these ingredients were well known in the art for use in bone growth mediums/explants.

Claims 1-8, 10 and 28-29 remain rejected and claims under 35 U.S.C. 103(a) as being unpatentable over Kwan et al. (US 6,187,047 B1) in view of Constantz (US 5,047,031) for the reasons of record.

Applicant states that "there is no motivation to combine Constantz and Kwan because Constantz is silent regarding the impact of acidic pH on bone growth protein

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induced bone formation. Moreover, Constantz provides no evidence that acidic pHs could enhance bone growth protein induced bone formation" (p. 10, Arguments).

However, as stated by the Examiner in previous Office Actions, it is clear that although Constantz did not recognize the advantage of the composition being at a pH from about 5-8, the pH was none-the-less within or overlapping this range. 'An acidic pH capable of enhancing bone growth protein induced bone formation' is disclosed by Constantz, because Constantz already taught pH's within, or overlapping the claimed ranges.

Because Constantz clearly taught that the composition comprising acidic calcium phosphates such as brushite would have had a pH of about 5-8, wherein a pH of 5-6 is considered 'acidic', the addition of brushite itself renders obvious 'an acidic pH capable of enhancing bone growth protein induced bone formation.

Although, as Applicant states, the references are not combined based solely upon pH, it is deemed that the combination of elements as listed in the claims is obvious over the prior art references (as keenly pointed out in the previous Office Actions).

Although neither reference specifically taught 'an acidic pH capable of enhancing bone growth protein induced bone formation', one of ordinary skill in the art would have none-the-less been motivated to combine the references because each element; a substrate, bone growth protein, calcium and phosphate were known in the art for aiding in bone growth. Therefore, one of ordinary skill in the art would have been motivated to combine brushite with a bone growth protein and a substrate in order to produce the

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formation of bone and the pH of brushite, which is acidic, is an intrinsic property of brushite.

Applicant argues "Applicant strongly disagrees with the Examiner's contention that Applicant's evidence shows merely a linear effect of acidic calcium phosphates in combination with bone growth proteins, relative to either class of compounds alone. Applicant submits that acidic calcium phosphates have an unexpected synergistic effect on the activity of bone growth proteins" (p. 10, Arguments).

However, the Instant specification provides no evidence of synergism. Synergism is an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients. It cannot be determined, from the examples presented in the Specification that the compositions provide evidence of synergism i.e., A alone, B alone and A+B together which would provide for an unexpected result.

Applicant argues that "...acidic calcium phosphates to be inferior, or at best equivalent, to basic calcium phosphates in bone repair applications...one of ordinary skill in the art beginning with the art-supported presupposition that the acidity of a calcium phosphate has either a negative or negligible impact on bone repair would necessarily find the superior explant masses.....to be 'surprising and unexpected'.

However, First, Applicant has not provided a solid basis for the contention that 'the acidity of calcium phosphate has either a negative or negligible impact on bone repair' especially since the prior art makes it well known that calcium phosphate does aid in bone repair. Because calcium phosphate aids in bone repair, it would be expected that a bone composition comprising calcium phosphate and bone growth proteins as well as known substrates would have also aided in bone repair. Further, it is pointed out that arguments pertaining to wherein the prior art perceived calcium phosphate as the inferior bone mineral for bone repair were not found convincing. For example, in the Declaration filed by Kevin J. Thorne on 5/18/04 indicates that 1) US 5,741,329 taught that taught the "deleterious effects of lowered pH in the vicinity of an implantable polymeric device". However, this example is does not bear a reasonable correlation to the claimed invention because the claimed invention does not impart a polymeric device – Although Mr. Thorne indicated that a lowered pH could disrupt bioactive compounds, this does not clearly indicate that acidic calcium phosphates would have been considered the inferior bone mineral compound and 2) US 5,525,148 taught "calcium phosphate is generally desirable in osteogenic compositions because it is the principal mineral component of teeth and bones....It is well known that hydroxyapatite is alkaline". However (2) does not indicate that acidic monophosphates are not beneficial in aiding in bone repair in the presence of bone growth proteins; (2) simply stated the preferred embodiment of '148.

Applicant has not pointed out any specific values that would be unexpected over the prior art, or which compounds provided for any synergistic results. Further, no data can be found which demonstrates that the acidity of the compounds actually has any unexpected results. Again, it is deemed that the inclusion of acidic calcium phosphates into a bone composition comprising *known* bone construction additives such as collagen and bone proteins would have been obvious to one of ordinary skill in the art because all of the ingredients were known to aid in bone repair. **The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.** See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No Claims are allowed.

This is an RCE of applicant's earlier Application No. 09/746,921. All claims are drawn to the same invention claimed in the earlier application and could have been

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finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

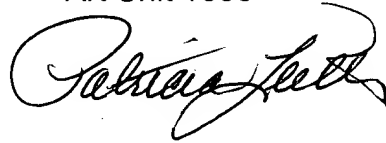
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia Leith
Primary Examiner
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A handwritten signature in black ink, appearing to read 'Patricia Leith', written in a cursive style.

07/21/05